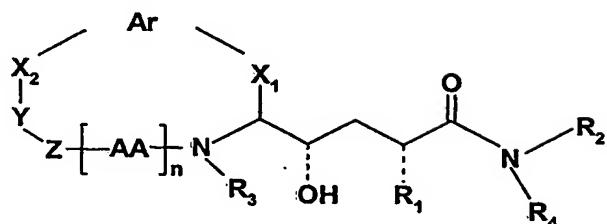


Claims:

## 1. A compound of formula I



wherein

- R<sub>1</sub> is (C<sub>1-8</sub>)alkyl, (C<sub>1-4</sub>)alkoxy(C<sub>1-4</sub>)alkyl, hydroxy(C<sub>1-6</sub>)alkyl, (C<sub>1-4</sub>)alkylthio(C<sub>1-4</sub>)alkyl, (C<sub>1-6</sub>)alkenyl, (C<sub>3-7</sub>)cycloalkyl, (C<sub>3-7</sub>)cycloalkyl(C<sub>1-4</sub>)alkyl, piperidinyl or pyrrolidinyl,
- R<sub>2</sub> and R<sub>4</sub>, independently, are hydrogen or optionally substituted (C<sub>1-8</sub>)alkyl, (C<sub>3-7</sub>)cycloalkyl, (C<sub>3-7</sub>)cycloalkyl(C<sub>1-4</sub>)alkyl, aryl, aryl(C<sub>1-4</sub>)alkyl, heteroaryl or heteroaryl(C<sub>1-4</sub>) alkyl, or
- R<sub>2</sub> and R<sub>4</sub>, together with the nitrogen to which they are attached, form an optionally substituted piperidino, pyrrolidinyl, morpholino or piperazinyl group,
- R<sub>3</sub> is hydrogen or (C<sub>1-4</sub>)alkyl,
- X<sub>1</sub> is CH<sub>2</sub>,
- X<sub>2</sub> is CH<sub>2</sub>, O, S, CO, COO, OCO, NHCO, CONH, or NR, R being hydrogen or (C<sub>1-4</sub>)alkyl,
- Y is (C<sub>1-8</sub>)alkylen or (C<sub>1-8</sub>)alkylenoxy(C<sub>1-6</sub>)alkylen, (C<sub>1-8</sub>)alkenylen or (C<sub>1-8</sub>)alkenylenoxy(C<sub>1-6</sub>)alkylen,
- Ar is a phenyl ring optionally mono- di- or trisubstituted by, independently, hydroxy or halogen, whereby X<sub>1</sub> and X<sub>2</sub> are in meta or para position to each other, and either
- Z is CO,
- AA is a natural or unnatural alpha-amino-acid, and
- n is 0 or 1,
- or
- Z is SO<sub>2</sub>,
- AA is an optionally substituted ethylenecarbonyl group (derived from a natural or unnatural alpha-amino acid by replacement of the nitrogen by a methylen group), and

n is 1

in free base or acid addition salt form.

2. A compound of formula I according to claim 1, wherein

$R_1$  is  $(C_{1-8})alkyl$ ,  $(C_{1-4})alkoxy(C_{1-4})alkyl$ ,  $hydroxy(C_{1-6})alkyl$ ,  $(C_{1-4})alkylthio(C_{1-4})alkyl$ ,  $(C_{1-6})alkenyl$ ,  $(C_{3-7})cycloalkyl$ ,  $(C_{3-7})cycloalkyl(C_{1-4})alkyl$ , piperidinyl or pyrrolidinyl,  $R_2$  and  $R_4$ , independently, are

- (a) hydrogen
- (b)  $(C_{1-8})alkyl$ ,  $(C_{3-7})cycloalkyl$  or  $(C_{3-7})cycloalkyl(C_{1-4})alkyl$ , in each case optionally substituted by one to three groups selected from hydroxy,  $hydroxy(C_{1-4})alkyl$ ,  $(C_{1-4})alkoxy$ ,  $(C_{1-4})alkoxy(C_{1-4})alkyl$ ,  $(C_{1-4})alkoxy(C_{1-4})alkoxy$ ,  $(C_{1-4})alkylsulfanyl$ ,  $(C_{1-4})alkoxycarbonyl$ ,  $(C_{1-4})alkylcarbonyloxy$ ,  $(C_{1-4})alkylcarbonyl-amino$ ,  $(C_{1-4})alkylcarbonyl$ ,  $(C_{1-4})sulfonyl$ , cyano, oxo, hetero  $(C_{3-7})cycloalkyl$  or heteroaryl, or
- (c) aryl, aryl $(C_{1-4})alkyl$ , heteroaryl or heteroaryl $(C_{1-4})alkyl$ , wherein in the latter two radicals heteroaryl denotes an aromatic 5- or 6- membered ring in which 1, 2 or 3 atoms are heteroatoms independently selected from O, N and S, wherein all radicals are optionally substituted by one to three groups selected from halogen, hydroxy, cyano, trifluoromethyl, carboxy,  $(C_{1-4})alkyloxycarbonyl$ ,  $(C_{1-4})alkylcarbamoyl$ ,  $(C_{1-4})alkylsulfonyl$ ,  $(C_{1-4})alkylcarbonyloxy$ ,  $(C_{1-4})alkylcarbonyl$ ,  $(C_{1-4})alkyl$ ,  $(C_{1-4})alkoxy$  or  $hydroxy(C_{1-4})alkyl$ , or

$R_2$  and  $R_4$ , together with the nitrogen to which they are attached, form an piperidino, pyrrolidinyl, morpholino or piperazinyl group, each of which is optionally substituted by one to three groups selected from hydroxy,  $hydroxy(C_{1-4})alkyl$ ,  $(C_{1-4})alkoxy$ ,  $(C_{1-4})alkoxy(C_{1-4})alkyl$ ,  $(C_{1-4})alkoxy(C_{1-4})alkoxy$ ,  $(C_{1-4})alkylsulfanyl$ ,  $(C_{1-4})alkoxycarbonyl$ ,  $(C_{1-4})alkylcarbonyloxy$ ,  $(C_{1-4})alkylcarbonylamino$ ,  $(C_{1-4})alkylcarbonyl$ ,  $(C_{1-4})sulfonyl$ , cyano, oxo, hetero  $(C_{3-7})cycloalkyl$  or heteroaryl,  $R_3$  is hydrogen or  $(C_{1-4})alkyl$ ,  $X_1$  is  $CH_2$ ,  $X_2$  is  $CH_2$ , O, S, CO, COO, OCO, NHCO, CONH, or NR, R being hydrogen or  $(C_{1-4})alkyl$ ,  $Y$  is  $(C_{1-8})alkylen$  or  $(C_{1-8})alkylenoxy(C_{1-6})alkylen$ ,  $(C_{1-8})alkylen$  or  $(C_{1-8})alkylenoxy(C_{1-6})alkylen$ ,

Ar is a phenyl ring optionally mono- di- or trisubstituted by, independently, hydroxy or halogen, whereby  $X_1$  and  $X_2$  are in meta or para position to each other, and either

Z is CO,

AA is a natural or unnatural alpha-amino-acid, and

n is 0 or 1,

or

Z is  $\text{SO}_2$ ,

AA is an optionally substituted ethylenecarbonyl group (derived from a natural or unnatural alpha-amino acid by replacement of the nitrogen by a methylen group), and

n is 1

in free base or acid addition salt form.

3. A compound of formula I according to claim 1, wherein

$R_1$  is  $(\text{C}_{1-4})\text{alkyl}$ ,

$R_2$  is  $(\text{C}_{1-6})\text{alkyl}$ ,

$R_3$  is hydrogen or  $(\text{C}_{1-4})\text{alkyl}$ ,

$R_4$  is hydrogen,

$X_1$  is  $\text{CH}_2$ ,

$X_2$  is  $\text{CH}_2$  or O,

Y is  $(\text{C}_{1-6})\text{alkylen}$ ,

Ar is unsubstituted phenylen, whereby  $X_1$  and  $X_2$  are in meta position to each other, and either

Z is CO,

AA is a natural or unnatural alpha-amino-acid, and

n is 0 or 1,

or

Z is  $\text{SO}_2$ ,

AA is an optionally substituted ethylenecarbonyl group (derived from a natural or unnatural alpha-amino acid by replacement of the nitrogen by a methylen group), and

n is 1

in free base or acid addition salt form.

4. A compound of formula I according to any one of claims 1 to 3, wherein

$R_1$  is  $(C_{1-4})$ alkyl,

$R_2$  is  $(C_{1-6})$ alkyl,

$R_3$  is hydrogen or  $(C_{1-4})$ alkyl,

$R_4$  is hydrogen,

$X_1$  is  $CH_2$ ,

$X_2$  is  $CH_2$  or O,

$Y$  is  $(C_{3-6})$ alkylen,

$Ar$  is unsubstituted phenylen whereby  $X_1$  and  $X_2$  are in meta position to each other, and either

$Z$  is CO,

$AA$  is  $-N(H)-CH(CH_3)_m-C(O)-$ , wherein  $m$  is 0 or 1 and

$n$  is 0 or 1,

or

$Z$  is  $SO_2$ ,

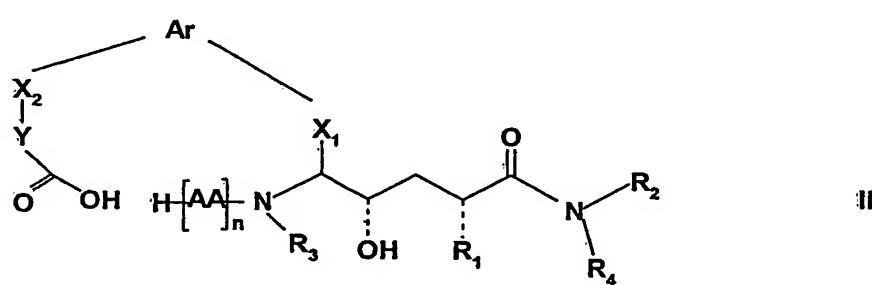
$AA$  is  $-CH_2-CH(CH_3)-C(O)-$  or  $-CH_2-CH_2-C(O)-$  and

$n$  is 1

in free base or acid addition salt form.

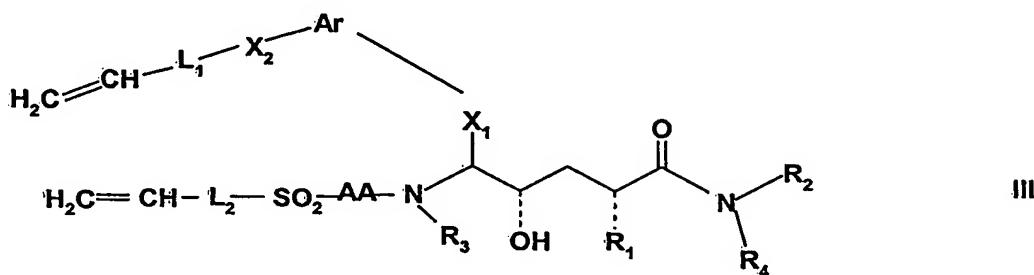
5. A process for the preparation of a compound of formula I as defined in claim 1, or a salt thereof, which includes the steps of

a) for the production of a compound of formula I wherein  $Z$  is CO, cyclisation by amide formation of a compound of formula II



wherein  $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_4$ ,  $X_1$ ,  $X_2$ ,  $Y$ ,  $Ar$ ,  $AA$  and  $n$  are as defined in claim 1,

b) for the production of a compound of formula I wherein Z is  $\text{SO}_2$  and Y is  $(\text{C}_{1-6})\text{alkenylen}$  or  $(\text{C}_{1-6})\text{alkylenoxy}(\text{C}_{1-6})\text{alkylen}$ , cyclisation by metathesis of a compound of formula III



wherein  $\text{R}_1$ ,  $\text{R}_2$ ,  $\text{R}_3$ ,  $\text{R}_4$ ,  $\text{X}_1$ ,  $\text{X}_2$ ,  $\text{Ar}$  and  $\text{AA}$  are as defined in claim I and  $\text{L}_1$  and  $\text{L}_2$ , independently are alkylen or alkylenoxyalkylen groups, or

c) for the production of a compound of formula I wherein Z is  $\text{SO}_2$  and Y is  $(\text{C}_{1-6})\text{alkylen}$  or  $(\text{C}_{1-6})\text{alkylenoxy}(\text{C}_{1-6})\text{alkylen}$ , hydrogenation of a compound of formula I wherein Z is  $\text{SO}_2$  and Y is  $(\text{C}_{1-6})\text{alkenylen}$  or  $(\text{C}_{1-6})\text{alkylenoxy}(\text{C}_{1-6})\text{alkylen}$ ,

and recovering the so obtained compound of formula I in free base or acid addition salt form.

6. A compound according to any one of claims 1 to 4 in free base or pharmaceutically acceptable acid addition salt form, for use as a pharmaceutical.
7. A compound according to any one of claims 1 to 4 in free base or pharmaceutically acceptable acid addition salt form, for use in the treatment of neurological and vascular disorders related to beta-amyloid generation and/or aggregation.
8. A pharmaceutical composition comprising a compound according to any one of claims 1 to 4 in free base or pharmaceutically acceptable acid addition salt form, in association with a pharmaceutical carrier or diluent.
9. The use of a compound according to any one of claims 1 to 4 in free base or pharmaceutically acceptable acid addition salt form, as a pharmaceutical, for the

treatment of neurological and vascular disorders related to beta-amyloid generation and/or aggregation.

10. The use of a compound according to any one of claims 1 to 4 in free base or pharmaceutically acceptable acid addition salt form, for the manufacture of a medicament for the treatment of neurological and vascular disorders related to beta-amyloid generation and/or aggregation.
11. A method for the treatment of neurological and vascular disorders related to beta-amyloid generation and/or aggregation in a subject in need of such treatment, which comprises administering to such subject a therapeutically effective amount of a compound according to any one of claims 1 to 4 in free base or pharmaceutically acceptable acid addition salt form.
12. A combination comprising a therapeutically effective amount of a compound according to any one of claims 1 to 4 in free base or pharmaceutically acceptable acid addition salt form and a second drug substance, for simultaneous or sequential administration.